

Bone Marrow Infiltration as the Primary Manifestation of Metastatic Melanoma: A Rare Case Report

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INTRODUCTION

Melanoma represents one of the most aggressive cutaneous malignancies. For the year 2024 in the United States, an estimated incidence of approximately 100,640 new cases and 8,290 deaths annually was reported; furthermore, it is projected to become the second most common cancer by 2040 [1]. This pathology exhibits an overall recurrence rate of 10.6%, regardless of the initial clinical stage, up to 30% of relapses occur within the first three years of diagnosis, 81% within five years, and 60% present as distant metastases[2]. The most frequent secondary sites are lung (30.7- 47.4%), liver (13.9 - 21.3%), bone (15.7%), and the central nervous system (10.8-31.6%). In contrast, bone marrow infiltration is an extraordinarily rare event, reported in a mere 5% to 7% of metastatic cases [3].

In the context of solid tumors, bone marrow involvement is unusual and confers a poor prognosis; although primarily associated with breast, lung, and prostate carcinomas, melanoma accounts for only 1.0% of these events [4]. The median survival for melanoma with bone marrow infiltration is merely two months [3], constituting one of the most catastrophic scenarios of metastatic disease. We present the case of a patient with massive bone marrow infiltration as a manifestation of aggressive recurrence, 11 years after the excision of a melanoma *in situ*. As far as we know, no similar cases have been reported in the indexed Mexican literature.

CASE PRESENTATION.

A 44-year-old male with a history of melanoma *in situ* the posterior cervical region, excised 11 years prior and reportedly under regular dermatological surveillance, presented to the emergency room. He reported a 10-day history of asthenia, adynamia, an unintentional weight loss of 4 kg, nocturnal diaphoresis, and lumbar pain radiating to the lower extremities. He received outpatient symptomatic treatment without improvement. Upon admission, vital signs were within normal limits, Physical examination was remarkable for scleral icterus, hepatosplenomegaly, and petechiae on the upper extremities.

Initial laboratory workup revealed severe thrombocytopenia and a leukoerythroblastic pattern in peripheral blood (4% blasts and 6 erythroblasts per 100 leukocytes), which was confirmed via peripheral blood smear. The liver function profile demonstrates a cholestatic pattern. Infectious and autoimmune etiologies were ruled out. During hospitalization, the patient experienced progressive deterioration of hepatic function. Imaging studies demonstrated hepatosplenomegaly (liver measuring 23cm and spleen 14 cm), multiple hypodense hepatic nodules, perivisceritis at the hepatic flexure of the colon, and free fluid in the abdominal cavity. Additionally, bilateral pleural effusion (predominantly right-sided) and multiple solid pulmonary nodules (The largest measuring 22x16mm) were identified.

Due to the onset of multi organ failure (Hepatic, renal, and pulmonary), the patient was transferred to the Intensive Care Unit (ICU) on the third day of admission. A bone marrow aspirate and biopsy were performed. Flow cytometry reported a hyper cellular marrow (90% viable cells) with a CD32+, CD117+, CD 13+. And CD33+ immunophenotype, initially interpreted as suggestive and myelodysplastic syndrome with 2.2% myeloid blast. Karyotype and genetic sequencing were normal, ruling out a primary lymphoproliferative process. On day 6 of admission, the patient developed multi organ failure requiring vasopressor support, acute kidney injury necessitating continuous kidney replacement therapy, and acute respiratory failure requiring endotracheal intubation. Despite advanced supportive measures and various administered therapies, the patient followed a fulminant course, progressing to cardiopulmonary arrest and dying on the seventh day of hospitalization.

The post-mortem histopathological result of the bone biopsy revealed a markedly hyper cellular bone marrow (85% cellularity) with massive infiltration by metastatic melanoma and extensive tumor necrosis. The immunohistochemical profile confirmed the diagnosis: SOX 10+, PRAME+, HMB45+ (patchy), and MiTF + (focal), accounting for 95%

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of the total cellularity, with persistence of remnant trilineage hematopoiesis. Hematolymphoid neoplasms and metastatic carcinomas were ruled out. A clinical autopsy was not authorized to characterize the cellular origin of the hepatic and pulmonary lesions.

DISCUSSION

Previous cohort studies (including follow-ups of patients with stage IA-IIIC cutaneous melanoma) indicate that tumor thickness (Breslow depth), ulceration, neurotropism, mitotic rate, and anatomic location are the primary predictors of recurrence. Primary tumors located on the scalp and neck carry up to a three-fold higher risk of recurrence compared to other anatomical regions [5]. In the present case, the initial anatomic site (neck) already represented an underestimated high-risk factor.

Bone marrow involvement is one of the rarest manifestations of metastatic melanoma occurring in only 5% to 7% of cases. In the medical literature, case reports of similar entities are typically characterized by a presentation featuring leukoerythroblastosis and fulminant clinical course. Other reported clinical and laboratory manifestations include pain (60.7%), anemia (80%), thrombocytopenia, and, in only 11% of cases, disseminated intravascular coagulation [3]. The literature reports fatal outcomes within one to three weeks following diagnosis [6]. Critically, our patient passed away before the definitive histopathological report was obtained (7 days from admission), underscoring the biological aggressiveness and rapid progression of this entity.

Although the overall five-year survival rate for *in situ* melanoma approaches 98.4%, documented sociodemographic disparities exist. Five-year survival rate can decrease by more than 10% in minority populations (Native Americans, Asians, African Americans, and Hispanics)[1], reflecting gaps in timely access to healthcare and long-term dermatological follow-up.

The absence of an ante-mortem diagnosis in this case was due to the atypical presentation of the tumor, which mimicked a primary hematologic malignancy (myelodysplastic syndrome), coupled with an unusually prolonged latency period (11 years) from a primary tumor traditionally considered low-risk (*in situ*). Due to the lack of a formal autopsy, it was not possible to confirm whether the hepatic and pulmonary nodules corresponded to the same cellular lineage, although clinical suspicion of systemic dissemination remains high.

CONCLUSIONES

This case represented a true diagnostic challenge due to its atypical hematologic presentation, and the prolonged latency period following the excision of the primary tumor. It is imperative to raise awareness among medical staff across all specialties that melanoma *in situ* should never be categorized as an innocuous entity. A history of this neoplasm demands permanent clinical suspicion and, potentially, the design of

extended clinical follow-up protocols. Furthermore, patients must be educated regarding the risk of late recurrence, the importance of skin self-examination, and the necessity of continuous medical surveillance.

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